REMARKS

The Office Action mailed March 1, 2002, has been received and carefully reviewed. Claims 1-62 have been canceled, claims 63-76 are withdrawn from consideration, and claims 77-90 are examined. Reconsideration and withdrawal of the rejections of the claims of the above-identified application is respectfully requested.

Rejections Under 35 U.S.C. §112, Second Paragraph

The claims have been amended in accordance with the Examiner's suggestions. Applicants submit that the claims as amended satisfy the requirements of 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. §102(e)

Claims 32-36, 38-40, 48, 49, 77-80, 82, 84 and 85 are rejected as being anticipated by Wondisford et al. (US 6,284,491). Wondisford et al. is asserted as teaching a labeled synthetic TSH receptor used to make antibodies for classic radioimmunoassay kits. Applicants respectfully traverse the rejection.

Wondisford is directed to recombinantly synthesising human TSH, and teaches assays and antibodies to TSH, not TSH receptors, as is instantly claimed. There is no teaching or suggestion in Wondisford of antibodies binding to the TSH receptor. As Wondisford fails to teach each and every element of the claims, withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §103(a)

Claims 32-34, 36, 37, 40, 41, 46-62 and 77-90 are rejected as being unpatentable over Bergmann (US 5,814,361) in view of Maclaren et al. (US 6,066,475). Bergmann is cited as teaching a method for measuring anti-TSH receptor autoantibodies (analyte) using a binder for the analyte and a competitor that also binds the binder. However, claims 77-90 require a TSH receptor with two distinct epitope regions, wherein the autoantibody analyte binds the first epitope but not the second epitope. The instant claims also require an antibody or fragment thereof that binds the second epitope. The

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antibody does not compete with the autoantibody for binding the same epitope region on the receptor.

Bergmann discloses a method for determining an analyte in a volume of a fluid sample and in particular for determining anti-TSH receptor autoantibodies in a patient serum. The method uses a binder (e.g. TSH receptor), a competitor (e.g. TSH), a solid phase having a substance (e.g. a first monoclonal antibody) for selective immobilization of the competitor not bound to the binder and a labeled reactant (e.g. a second monoclonal antibody, binding to an epitope region of the competitor distinct to the epitope region of the competitor binding to the first monoclonal antibody) for the immobilized competitor, so that the amount of competitor bound to the solid phase can be determined.

Bergmann is distinguished from the instant invention in many ways. Firstly, the first and second monoclonals of Bergmann are directed to epitopes of TSH and not to the TSH receptor. Secondly, the monoclonals of Bergmann and the binding properties thereof are characterized with respect to their binding to distinct epitopes of TSH and as such there is no disclosure or suggestion that an antibody should be produced binding to an epitope of a TSH receptor or fragment thereof that is not recognized by TSH receptor autoantibodies. Indeed the provision of such an antibody would seem to be unnecessary for a method as described in Bergmann. For example, immobilizing or labeling of a TSH receptor as is achieved by the use of an antibody that binds TSH receptor at a site different from the binding site of TSH in the present invention would not be required in Bergmann because immobilizing or labeling of TSH in Bergmann is achieved by means of the first and second monoclonals characterized by their binding to distinct epitopes of TSH.

Thirdly, while the Examiner asserts that "it is inherent that a TSH receptor is bound to the solid phase at some point in the assay" of Bergmann, Applicants have found no suggestion of this. In the assay of Bergmann, the immobilized monoclonal and the TSH receptor do not bind each other but bind to the same epitope of TSH, so that binding of the TSH receptor to TSH precludes binding of the immobilized antibody to TSH. In this way, the TSH receptor is not bound to the solid phase in Bergmann. Thus, Bergmann fails to teach or suggest the required elements of the claimed invention.

Maclaren does not supply what Bergmann lacks. Applicants respectfully request withdrawal of the rejection.

Claims 42-45 are rejected under 35 U.S.C. §103(a) as being unpatentable over Wondisford in view of Tanaka (US 5,639,627). Claims 42-45 have been canceled, rendering the rejection moot.

It is respectfully submitted that each of the presently pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' representative at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332.5300

Date: 9/3/02

Name: John J. Gresens
Reg. No.: 33,112
JJG/NJP

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MARKED-UP VERSION TO SHOW CHANGES MADE

Please cancel claims 1-62 and amend claims 77, 78, 82-84 and 88-90 to read as set forth below:

77. (Amended) A kit for use in screening a sample of body fluid for autoantibodies to (i) a thyroid stimulating hormone (TSH) receptor, or (ii) at least a TSH receptor fragment, which kit comprises:

(a) a source of (i) a TSH receptor or (ii) a TSH receptor fragment, said (i) TSH receptor or (ii) TSH receptor fragment each having at least first and second distinct epitope regions, wherein autoantibodies to said (i) TSH receptor or (ii) TSH receptor fragment bind to said first epitope region but not said second epitope region;

(b) at least one antibody, or fragment thereof, [capable of binding] that binds to said second epitope region of said (i) TSH receptor or (ii) TSH receptor fragment;

(c) means for contacting said (i) TSH receptor or (ii) TSH receptor fragment of (a) with at least said sample of body fluid being screened and said antibody of (b), whereby said contacting means allow:

autoantibodies when present in said sample of body fluid being screened to bind to said first epitope region of said (i) TSH receptor or (ii) TSH receptor fragment; and

said antibody of (b) to bind to said second epitope region of said (i) TSH receptor or (ii) TSH receptor fragment; and

(d) means for monitoring binding of said autoantibodies and said (i) TSH receptor or (ii) TSH receptor fragment, so as to provide an indication of the presence of autoantibodies to said (i) TSH receptor or (ii) TSH receptor fragment in said sample of body fluid being screened.

78. (Amended) A kit according to claim 77, wherein said antibody of (b) comprises a monoclonal antibody, or a recombinant antibody, or fragment thereof [capable of binding] that binds to said second epitope region of said (i) TSH receptor or (ii) TSH receptor fragment.

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82. (Amended) A kit according to claim 77, wherein said contacting means [are such as to] enables contact of said antibody of (b) with said (i) TSH receptor or (ii) TSH receptor fragment prior to contact of said (i) TSH receptor or (ii) TSH receptor fragment with said sample of body fluid being screened.

83. (Amended) A kit according to claim 77, wherein said contacting means [are such as to] enables contact of said antibody of (b) with said (i) TSH receptor or (ii) TSH receptor fragment concurrent with or after contact of said (i) TSH receptor or (ii) TSH receptor fragment with said sample of body fluid being screened.

84. (Amended) A kit according to claim 77, which further comprises a competitor [capable of binding] that binds with said first epitope of said (i) TSH receptor or (ii) TSH receptor fragment and whereby said contacting means [are such as to] enables contact of said competitor with said (i) TSH receptor or (ii) TSH receptor fragment[, said sample of body fluid being screened and said antibody of (b)].

88. (Amended) A kit according to claim 84, wherein said contacting means [are such as to] enables contact of said competitor with said (i) TSH receptor or (ii) TSH receptor fragment after contact of said (i) TSH receptor or (ii) TSH receptor fragment with said antibody of (b).

89. (Amended) A kit according to claim 84, wherein said contacting means [are such as to] enables contact of said competitor with said (i) TSH receptor or (ii) TSH receptor fragment before or concurrent with contact of said (i) TSH receptor or (ii) TSH receptor fragment with said antibody of (b).

90. (Amended) A kit according to claim 77, which further comprises a binding agent specific for said autoantibodies present in said sample of body fluid being screened and whereby said contacting means [are such as to] enables contact of said binding agent

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with said [(i) TSH receptor or (ii) TSH receptor fragment,] autoantibodies present in said sample of body fluid being screened [and said antibody of (b)].

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